1. (amended) A variant human MLH1 or MSH2 gene comprising hMLH1 mutant 1, [hMLH1 mutant 2,] hMSH2 mutant 1, hMSH2 mutant 2 or hMSH2 mutant 3.

Please cancel claims 4, 5, 6, 7 and 8 without prejudice.

REMARKS

Claims 1-8 are pending in the instant application. Claims 1-8 have been rejected. Claim 1 has been amended. Claims 4, 5, 6, 7 and 8 have been canceled. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Objection to Claim 1

Claim 1 has been objected to as not complying with sequence rule 37 C.F.R. 1.821(d). This rule requires that when a claim discusses a sequence that is set forth in the "Sequence Listing" reference to the sequence must be made using the sequence identifier preceded by "SEQ ID NO:". It is respectfully pointed out, however, that claim 1 is not drawn to sequences set out in the Sequence Listing. Instead, claim 1 is drawn to mutants

specifically defined in the specification at pages 15-17. Accordingly, sequence rule 37 C.F.R. § 1.821(d) is not applicable to claim 1 and withdrawal of this objection is respectfully requested.

II. Rejection of Claim 8 under 35 U.S.C. § 101

Claim 8 has been rejected under 35 U.S.C. § 101 as the Examiner suggests that the claimed invention is directed to nonstatutory subject matter. Specifically, the Examiner suggests that claim 8 encompasses any transgenic organism, including a human being.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have canceled claim 8. Withdrawal of this rejection is therefore respectfully requested.

III. Rejection of Claim 8 under 35 U.S.C. § 112, first paragraph

Claim 8 has been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claim 8 has also been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have canceled claim 8. Withdrawal of these rejections under 35. U.S.C. § 112, first paragraph, is therefore respectfully requested.

IV. Rejection of Claims 1-4, 6 and 8 under 35 U.S.C. § 112, second paragraph

Claims 1-4, 6 and 8 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 1, the Examiner suggests that it is unclear with respect to the nucleotide sequences cited because they do not include a SEQ ID NO:. The Examiner suggests that sequence databases indicate that there are multiple sequence listings for the human. Applicants respectfully disagree.

At the outset, it is respectfully pointed out, that definiteness of claim language must be analyzed, not in a vacuum, but in light of: (A) The content of the particular application disclosure; (B) The teachings of the prior art; and (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. See MPEP § 2173.02.

hMLH1 mutant 1, hMSH2 mutant 1, hMSH2 mutant 2 and hMSH2 mutant 3 are defined in the specification at page 17, lines 1-14, wherein the specific mutations of each mutant with respect to hMLH1 or hMSH2 are outlined. Further, at page 1, line 26, through page 2, line 5, references teaching the hMLH1 and hMSH2 genes to which the mutants are compared are listed. Thus, what is meant by hMLH1 mutant 1, hMSH2 mutant 1, hMSH2 mutant 2 and hMSH2 mutant 3 would be clear to one of skill in the art when read in light of the teachings of the instant application and the prior art cited therein. Thus, claim 1 meets the requirements of 35 U.S.C. § 112, second paragraph.

Claims 2 and 3 are suggested to be unclear and incomplete in the recitation of "the presence of the variant gene is indicative of a susceptibility to hereditary non-polyposis colorectal cancer" because method steps are not present that indicate which mutants

correspond to a predisposition to colorectal cancer. Applicants respectfully disagree.

Claims 2 and 3 are dependent from claim 1 which is drawn to specific mutants, all of which are defined in the specification as being useful in diagnosing HNPCC in a patient and determining susceptibility of a patient for developing HNPCC. See, for example, page 17, lines 14-16. Claims 2 and 3 are drawn to methods wherein a DNA sample of a patient is screened for one of these specific mutants. Thus, an additional method step indicating which mutants correspond to a predisposition to colorectal cancer is unnecessary to complete the claims as detection of any of the specified mutants is indicative of this predisposition.

Claims 4 and 6 are suggested to be unclear and incomplete in the recitation of "identifying mutants in splice donor or acceptor sites" because the method steps are not present that indicate the base pair changes in the claimed splice mutants. It is respectfully pointed out that claims 4 and 6 have been canceled, thus mooting this rejection.

Claim 8 is also suggested to be vague and indefinite in recitation of "system". As discussed in previous sections, however, claim 8 has been canceled, thus mooting this rejection.

Withdrawal of these rejections under 35 U.S.C. § 112, second paragraph, is respectfully requested in light of the amendments to the claims and the above arguments.

V. Rejections of Claims 1-7 under 35 U.S.C. § 102(a), (b) and (e)

Claims 1-7 have been rejected under 35 U.S.C. § 102(a) as being anticipated by Farrington et al. The Examiner suggests that Farrington et al. teach the same mutants as in the instant invention, as well as the methods and primers to detect the mutants. It is respectfully pointed out, however, that the reference by Farrington et al. is not the invention of another but rather is the inventors' own work. Applicants are providing herewith a Declaration by co-inventor Juili Lin Goerke establishing the contributions of each co-author of this paper. As discussed in detail in this Declaration, while the co-authors Susan M. Farrington, Yute Wang, John D. Burczak, and Malcolm G. Dunlop, contributed technically to the experiments reported in this references, they are not inventors of the instant claimed invention. Accordingly, since the Farrington et al. reference is not by "another", it is not a valid prior art reference for purposes of 35 U.S.C. § 102(a). Withdrawal of this rejection is therefore respectfully requested.

Claims 2-7 have also been rejected under 35 U.S.C. § 102(b) as being anticipated by Weber et al. The Examiner suggests that Weber et al. teach a method and the appropriate primers to do genomic sequencing of MLH1 and MSH2 and detect mutations predictive of hereditary nonpolyposis colorectal cancer. Further, the Examiner suggests that the mutation which results in the deletion of exon 13 in patient 817, MLH1 mutant 2, was described by Liu et al. 1995 and Dunlop et al. 1997.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended claim 1 to no longer include hMLH1 mutant 2. Further claims 4, 5, 6, and 7 have been canceled, thus mooting this rejection as it pertains to these claims.

With respect to claims 2 and 3, however, Applicants respectfully traverse this rejection. Claims 2 and 3 are drawn to methods of diagnosing hereditary non-polyposis colorectal cancer or predicting susceptibility of a patient to developing hereditary non-polyposis colorectal cancer via screening a DNA sample for hMLH1 mutant 1, hMSH2 mutant 1, hMSH2 mutant 2 or hMSH2 mutant 3. None of the cited prior art references teach these mutants of hMLH1 or hMSH2. Accordingly, these references cannot anticipate the claims as now presented.

Withdrawal of this rejection under 35 U.S.C. § 102(b) is therefore respectfully requested.

Claims 2-8 have also been rejected under 35 U.S.C. § 102(e) as being anticipated by Liskay et al. As discussed above, claims 4, 5, 6, 7 and 8 have been canceled thus mooting this rejection as it pertains to these claims. With respect to claims 2 and 3, Applicants respectfully traverse this rejection.

Claims 2 and 3 are drawn to methods of diagnosing hereditary non-polyposis colorectal cancer or predicting susceptibility of a patient to developing hereditary non-polyposis colorectal cancer via screening a DNA sample for hMLH1 mutant 1, hMSH2 mutant 1, hMSH2 mutant 2 or hMSH2 mutant 3. Liskay does not teach these mutants of hMLH1 or hMSH2. Accordingly, since this reference does not teach all the elements of the claimed invention, it cannot anticipate the claims. See MPEP § 2131. Further, since this reference neither teaches nor suggests all the limitations of the claimed invention, it cannot render obvious the instant claims. See MPEP § 2142.

Withdrawal of this rejection under 35 U.S.C. § 102(e) is therefore respectfully requested.

VI. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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